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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,707	10/27/2005	Masataka Kuwana	4439-4036	2198

27123 7590 12/16/2008

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
12/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/549,707	KUWANA ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-16,19,20 and 22* is/are pending in the application.

4a) Of the above claim(s) *9-16,19,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. The amendment filed on 29 August 2008 has been entered into the record and has been fully considered.

2. Claims 2-8 are amended.

3. Claims 2-8, drawn to a monocyte-derived multipotent cell expressing CD14, CD34, CD45 and type I collagen, are being considered for examination in the instant application, are under consideration in the instant application.

Response to Amendment

Withdrawn objections and/or rejections

4. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (29 August 2008).

5. The rejection of claims 2-8 under 35 U.S.C. § 102(a) and 102(e) is withdrawn in view of claim amendments and Applicant's persuasive argument.

Rejection maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. The rejection of claims 2-8 under 35 U.S.C. 102(b) as clearly anticipated by Zhao et al., (PNAS 100: 2426-2431, 2003), is applied to the amended claims as rejected under 35 U.S.C. 102(a), for reasons of record in the Office Action dated 2 May 2008. The Examiner apologizes for a typographical error in the earlier rejections submitted under 102(b) instead or 102(a). Any inconvenience caused therein is regretted.

7. Based upon PTO's suggestion and guidelines discussed during the interview dated 12 August 2008, Applicants amend claims to remove the phrase "is capable of differentiating", replace the term "monocyte" with "monocyte-derived multipotent cell (MOMC), and insert "MOMC" in the instant claims. All amendments are considered and acknowledged.

8. Applicant asserts that the amendment of claim 2 to recite "monocyte-derived multipotent cell (MOMC)" instead of "monocyte" presents a process step of obtaining MOMC by culturing PBMC in vitro on fibronectin and collecting

fibroblast-like cells expressing CD14 and CD34. Applicant argues that the instantly claimed process is different from Zhao's process, primarily for 2 reasons: (i) Zhao obtains pluripotent stem cells (PSC) by repeated stimulation of PBMC with macrophage-colony stimulating factor (M-CSF) and phorbol myristate acetate (PMA). (ii) Zhao cells have different differential potential or functional characteristics. Applicant provides the Seta reference for evidence on the uniqueness of the MOMC, asserting that the reference details the criticality of the methods, and a significance of using fibronectin or M-CSF/PMA in cultures. Furthermore, pointing to the Examiner cited Blau reference Applicants argue that Blau essentially teaches that the "functional characteristics of the cell are critical in determining the cell identity". Applicant's attempts to induce MOMC with different factors used by Zhao, e.g. IL-2 factor, nerve growth factor or epidermal growth factor, for differentiation to T-cells, neuronal cells and epithelial cells, respectively as shown by Zhao, resulted in failure. Applicants, therefore, allege that undue experimentation would be required of a skilled artisan to use Zhao's PSC and derive at the claimed MOMC having the same functional characteristics. Applicants, therefore, conclude that the PSC of Zhao is distinct from the claimed MOMC, and that Zhao does not anticipate the claimed invention. Also because Zhao does not disclose each and every element of the claims, Applicants request reconsideration and withdrawal of the rejection.

9. Applicant's arguments are fully considered, however, are not found to be persuasive. Examiner acknowledges Applicant's claim amendment replacing

"capable" with a more definitive term "differentiates". However, as stated in the previous Office Action, the claims still read as product-by-process claims, and as set forth in MPEP Chapter 2113:

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Therefore, product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. As explained earlier, the method steps recited in the instant claims neither relate to the claimed multipotent cells, nor imply any structural limitations to the product. Moreover, MOMC and PSC cells are structurally similar and express the same markers as claimed, and additionally are multipotent or pluripotent stem cells having the potential of differentiation to various cell lineages. Furthermore, the publication submitted by Applicant (Seta and Kuwana) provides evidence that PSC and MOMC are structurally the same because both cell types express CD14, CD34 and CD45 (Table 1). Because the expression of type I collagen is indicated as "N/D" and not "-" (N/D is not defined in the article) for PSC, Examiner interprets N/D as not determined; that is, not tested. That the references (Zhao and Seta)

are silent on the positive expression of collagen type I, does not prove otherwise, absent evidence to the contrary.

10. Additionally, contrary to Applicant's assertion, the Seta reference does not disclose the significance of using fibronectin, or M-CSF/PMA. The reference plainly states that Zhao uses M-CSF/PMA for repeated stimulation of PBMC. As adjudged from the discussion above and in prior Office Actions, the claim recites a product by process. Applicants are claiming the MOMC product which is derived from the same source, and express the same markers, as Zhao's PSC. Neither the Seta disclosure nor the instant specification provides sufficient guidance on the significance of fibronectin in the culture process that result in a unique cell product. The role of fibronectin is rather non-specific and unclear. For example, monocytic EPC cells cultured on fibronectin or collagen type I, demonstrate the same morphology, cellular markers and differentiation ability as MOMC (see Table 1 of Seta reference). However, Applicant's attempts to induce MOMC using collagen type I resulted in failure of differentiation potential.

11. Citing the Blau reference, Applicant allege that Blau teaches that a stem cell is not a specific cellular entity, rather a function that "can be assumed by numerous diverse cell types". Applicant, therefore, asserts that MOMC and PSC are different cells based on the functional characteristics of each cell type. This argument is persuasive in part, because cellular differentiation can also depend on culture conditions and environmental cues, thereby indicating a dynamic feature. For example, Seta et al. teach that "distinct differentiation potentials of

these primitive cells might be due to different culture conditions of the same precursors" (primitive cells correspond to monocyte derived cells) (page 46, para 1). This corroborates with the Blau statement in the earlier Office Action that adult stem cells and progenitor cells are not unique and compartmentalized to differentiation to specific cell types expressing specific markers. Blau et al further teach that stem cells can give rise to various cell lineages and tissues depending on the microenvironmental cues, growth factors, differentiation factors, etc., by virtue of plasticity, heterogeneity and transdifferentiation characteristics (Figs 1, 7, 8). For example neural stem cells can form skeletal muscle, bone marrow derived stem cells can form multiple tissues, and cells from various tissues can give rise to bone marrow cells (page 837, para 1). Hence PSC of Zhao et al and the instant MOMC, both being multipotent or pluripotent stem cells, both having derived from the same source and expressing the same markers, have similar differentiation potential based upon the Blau teaching.

12. Finally to provide proof that the Zhao cells are different from the instant MOMC, Applicant demonstrates data showing that MOMC cultured under Zhao conditions do not differentiate to neurons, hepatocytes, or epithelial cells. However, in order to reproduce Zhao result and present a comparison with the instant MOMC, Applicants require to conduct a complete study following the Zhao and instant protocol. As explained above, Zhao's PSC are structurally the same as MOMC, therefore, the cells of the prior art would be functionally the same under identical culture conditions, absent evidence to contrary. Applicant's

data do not support such information because Applicant's comparison is incomplete, therefore, inconclusive.

Conclusion

13. No claims are allowed.

14. **THIS ACTION IS MADE FINAL.**

15. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

17. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
07 December 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649